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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/055,106	01/23/2002	Lee Harland	PC10970AGLK	9647

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EXAMINER	
SHUKLA, RAM R	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/055,106	HARLAND, LEE	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above claim(s) *16-18 and 25-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/4/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of the invention of group I, claims 1-15 and 19-24, drawn to a polynucleotide encoding a GPCR polypeptide in Paper filed 2-6-2004 is acknowledged. The traversal is on the ground(s) that the examiner has not met the requirement that the search and examination of the entire application will cannot be carried out without serious burden. This is not found persuasive because the previous office action discussed why the searches for the different inventions would not be coextensive. For example, search of a nucleic acid would not yield an art relevant to a protein. Additionally, examination of a nucleic acid would not require the same considerations as those for examining a protein as discussed in the previous office action of 12-22-2003.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 16-18 and 25-43 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper filed 2-6-2004.

3. Claims 1-43 are pending.

4. Claims 1-15 and 19-24 are under consideration.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-15 and 19-24 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

When the claims are analyzed in light of the specification, instant invention encompasses (i) any polynucleotide that encodes the polypeptide of SEQ ID NO 2 (ii) the nucleotide sequence of SEQ ID NO 1, (iii) a nucleotide sequence that is at least 70-98% identical to the sequence of SEQ ID NO 1, (iv) any polynucleotide sequence that hybridizes to the sequences disclosed in (i)-(iii) and any fragment of the polynucleotides of (i)-(iv). The invention also encompasses cells comprising these polynucleotides and preparations from these cells.

However, the specification discloses only the nucleic acid disclosed in SEQ ID NO 1 which encodes the polypeptide disclosed in SEQ ID NO 2. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, SEQ ID NO 1 is the only species whose complete structure is disclosed. The specification does not provide any disclosure as to what would have been the sequence structure of the nucleic acids encompassed by (iii) – (iv). Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the no identifying characteristic of the sequences has been described. In regard to polynucleotides from species other than humans, it is noted that the specification does not provide any disclosure whether these sequences from other species would have had same characteristics would have had additional characteristics or properties.

Applicants' attention is directed to the decision in *In re Shokal*, 113 USPQ 283 (CCPA 1957) wherein is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of cDNAs besides SEQ ID NO 1 that encodes the amino acid sequences disclosed in SEQ ID NO 2, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-15 and 19-24 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

When determining whether an applicant has described the utility of invention, one has to determine whether the applicant has described a well-established utility. If not, has the application made any assertion of specific, substantial and credible utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for use. In contrast to general utility, a specific utility will be specific to the claimed subject matter. A substantial utility defines a real world utility of the invention and utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context use are not substantial utility (see utility guidelines, in Federal Register January 5, 2001, Volume 66, Number 5, Pages 1092-1099).

In case of an isolated DNA, when the major utility of the DNA is as a probe, it is asked if the DNA is specific to a particular organism or is it discriminatory towards a certain organism. For example, if said DNA was used as probe, one can identify an organism with certainity. In other words, it will specifically hybridize to

the genome of a certain organism. In case of DNA encoding protein claims, one asks whether the protein has an established and specific biological function.

The instant invention is not considered to have a specific and/or substantial utility because the specification fails to establish that the disclosed nucleic acid sequence encodes a GPCR as shown by structural and functional properties. The recited SEQ ID NO is simply computer generated hypothetical open reading frames, wherein no biological function has been established. It is known in the art that the G protein coupled receptors have very divergent functions (see specification on page 1, lies 15-30). However, the specification fails to show a single working example that establishes that the instantly claimed nucleic acid encodes a GPCR, and what is its biological function. The specification alleges that according to BLAST search, the closest protein match of the protein sequence encoded by SEQ ID NO 1 was to a Cysteinyl Leukotriene Receptor (CYSTLT1) (figure 3), however, the specification does not provide any disclosure as to what percent of identity was present between the two proteins. The specification does not provide any specific information as to what type of functional domains or motifs present of conservation are present in the polypeptide encoded by the claimed nucleic acid. Therefore the specification fails to teach that the polypeptide encoded by SEQ ID NO 1 has the biological activity of a GPCR, explicitly or implicitly as putatively considered by the specification. Even if the sequence comparison results show that the claimed nucleotide encodes a GPCR, there is no evidence as to what is the function of the protein or the specification does not teach any assay method for assaying the function of the encoded protein. It is emphasized that GPCRs are a superfamily of several hundred members which can be classified into families and subfamilies. Table 1 in Morris and Malbon (Physiological Reviews 79:1373-1430, 1999) lists known GPCRs at that time and this table indicates how diverse GPCRs in function. In other words, the only immediate apparent utility for the instant invention would be its further scientific characterization as a putative GPCR.

Therefore, the asserted use for the claimed nucleic acid is not considered to support by either a specific and/or substantial utility, since no function can be ascribed to the gene.

9. Claims 1-15 and 19-24 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/or substantial utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. Claims 1-15 and 19-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In addition to the issues raised in the utility rejection, the claimed invention is not enabled for reasons set forth below. If the utility rejection was to be withdrawn these rejections would remain.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

When the claims are analyzed in light of the specification, instant invention encompasses (i) any polynucleotide that encodes the polypeptide of SEQ ID NO 2 (ii) the nucleotide sequence of SEQ ID NO 1, (iii) a nucleotide sequence that is at least 70-98% identical to the sequence of SEQ ID NO 1, (iv) any polynucleotide sequence that hybridizes to the sequences disclosed in (i)-(iii) and any fragment of the polynucleotides of (i)-(iv). The invention also encompasses cells comprising these polynucleotides and preparations from these cells.

As discussed in the utility rejection, there is no guidance and evidence in the specification that the claimed nucleic acid encodes a GPCR, what is its biological function, how to test its biological function and how to make the polynucleotides encompassed by the claimed invention and how to use them. It is emphasized that GPCRs are a superfamily of several hundred members which can be classified into families and subfamilies. Table 1 in Morris and Malbon (Physiological Reviews 79:1373-1430, 1999) lists known GPCRs at that time and this table indicates how diverse GPCRs in function. While the specification, based on its blast analysis, indicates that it has sequence identity to CYSLT1, there is no guidance as to how related the two proteins are, what are the domain structures of the protein or whether the protein encoded by the claimed nucleic acid would have the same activity function as CYSLT1. The specification does not provide any guidance as to which parts of the two proteins are identical, to what extent and whether such identity or similarity is in functional domains. In summary, there is not evidence that the claimed nucleic acid would encode a protein that would have CYSLT1 like function or activity.

First, the specification is not enabling for all the claimed polynucleotides of claims 1 and host cells comprising said polynucleotides because the specification only teaches a polynucleotide that encodes a putative GPCR whose biological function is not known as discussed above. Even if its function was known, regarding the embodiments in claim 1 (c-e) and claims 2-8, the specification does not provide any evidence that such polynucleotide will encode a GPCR and what will be the function and whether they would have the putative biological activity. For example will a polynucleotide in which up to 25% of the nucleotide sequences have

been altered would encode a functional protein that would have the biological activity and function of the wild type protein. These proteins would include mutants produced by deletion, substitution, and addition in the wild type polynucleotides such that up to 10% of nucleotides would be different from the sequence of SEQ ID NO 1. For example, SEQ ID NO 1 contains 918 nucleotides, which encodes for a protein of 305 amino acids. A change in 25% of this polynucleotide would be about 230 nucleotides that would encode about 76 amino acid. This would correspond to a change in every other amino acid of the polypeptide encoded by SEQ ID NO 1. It is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence, and the functional properties of the different parts of the protein (see second paragraph in Rudinger J in Peptide Hormones. Editor Parsons JA. Pages 1-7, 1976, University Park Press, Baltimore). Rudinger further add, "The significance of particular amino acids and sequences for different aspects of biological activity can not be predicted *a priori* but must be determined from case to case by painstaking experimental study" (see conclusion on page 6). The specification does not teach which changes in the nucleotide sequence of SEQ ID NO 1 would encode an amino acid sequences that would retain the putative function of the protein of SEQ ID NO 2. The specification does not teach how to use a nucleic acid that would have encoded a protein, which was derived from the protein of SEQ ID NO 2 but did not have the function of the starting protein. Alternatively, the specification does not teach how would an artisan have made a polynucleotide that would have encoded a protein in which every other amino acids would have been changed but the protein would have retained the function of the starting protein.

Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant amino acid substitutions and the nature and extent of changes that can be made in these positions in order to obtain protein that retain function. Such a definition might also read on previously characterized proteins, or alternatively, might include

proteins with additional functions or activities neither envisioned nor enabled by applicants in the current invention.

As set forth in *In re Fisher,* 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Even if these polynucleotides were to be used as a probe and the 25% change in the nucleotide sequence was to be spread across the entire length of the polynucleotide, they will not be able to specifically recognize a related polynucleotide or the polynucleotide of SEQ ID NO 1. Likewise, the polynucleotides that have up to 25% nucleotides changed would not be functional in a diagnostic assays because they would not recognize the sequence of SEQ ID NO 1 in a sample under stringent hybridization conditions. If one used degenerate nucleotides for every amino acid in the protein, resultant polypeptide would not hybridize to a sequence of SEQ ID NO 1 in a biological sample and therefore, the diagnostic assay would not work. Alternatively, if it is not known whether the protein encoded by these polynucleotides did not have the biological activity, how can they be used in treating a patient or for treating what disease?

Additionally, if the specification is not enabling for the claimed polynucleotides, it would not be enabling for the claimed vectors or host cells comprising the polynucleotide or products isolated from the host cell because if an artisan did not know what was the function of the protein encoded by the claimed

polynucleotide, how would an artisan know, how to use such vectors or host cells that comprised such polynucleotides or vectors.

In summary, the specification as filed does not provide any guidance how to make and use the claimed polynucleotides, vectors, probes, host cells recited in the claims and an artisan of skill would have required undue experimentation to make and use the claimed invention because neither the art of record nor the specification teaches how to make and use the claimed invention as discussed above.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 2-15 and 19-24 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is noted that claims 2-15 and 19-24 are dependent claims that depend from claim 1 or other claims. These claims recite "a polynucleotide according to claim 1", "a process of claim 19" etc. even when the term "a polynucleotide" or "a process" has been recited before. The metes and bounds of the claimed invention is unclear since claim 1 recites "a polynucleotide" and it is unclear as to which polyucleotide is being referred to in claims 2-15 and 19-24. Use of the article "The" will be remedial for an embodiment in second or following recital of the embodiment.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for

> patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 1-15 and 19-24 have been rejected under 35 U.S.C. 102(e) as being anticipated by Chen et al (US Pub No. 2003/0139588 A9, 7-24-2003, effective filing date Nov 27, 2000).

The nucleic acid of SEQ ID NO 3 in Chen et al would encode the polypeptide of SEQ ID NO 2 of the instant application (see SEQ ID NO 3 on page 20 continued on page 21. The art also teaches the plasmid, vector, host cells comprising the vector (see paragraph 13 on page 2 (also see rest of the publication for detailed description of these embodiments, such as examples on pages 9-19).

15. Claims 1-15 and 19-24 have been rejected under 35 U.S.C. 102(e) as being anticipated by Chen et al (US Pub No. 2002/0193584 A1, 12-19-2002, effective filing date Nov 27, 2000).

The nucleic acid of SEQ ID NO 3 in Chen et al would encode the polypeptide of SEQ ID NO 2 of the instant application (see SEQ ID NO 3 on page 20 continued on page 21. The art also teaches the plasmid, vector, host cells comprising the vector (see paragraph 13 on page 2 (also see rest of the publication for detailed description of these embodiments, such as examples on pages 9-19).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (571) 272-0735 . The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or

proceeding should be directed to the William Phillips whose telephone number is (571) 272-0548.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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